ARGUMENTS/REMARKS

Rejection claims 2-8, 11-15, and 17 under 35 U.S.C. § 102(e)

Claims 2-8, 11-15, and 17 were rejected as anticipated by LaPosta.[1] For the reasons discussed below, the applicants respectfully traverse.

The applicants previously introduced claim 17, a product-by-process claim. The Office Action now asserts that the claim limitation "storing the liquid vaccine in the liquid state" is a process limitation in a product claim. Because the Office Action did not further elaborate, the applicants presume this phrase is not being considered as a distinguishing feature of the claims. The applicants respectfully disagree.

LaPosta teaches the making of a liquid composition comprising an antigen and a sugar that is immediately lyophilized. This is because at the time of LaPosta it was well recognized that liquid vaccine compositions change over time, their immunogenicity decreasing as a function of time. Accordingly, LaPosta teaches lyophilization of its liquid vaccine composition to prevent such diminution of immunogenicity.

The present inventors discovered that including trehalose in a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein will attenuate (but not halt) the rate at which the antigen's immunogenicity decreases with time. This enables one to store the vaccine composition in the liquid state and obviate the need for lyophilization and subsequent reconstitution.

Although the inclusion of trehalose in the presently claimed composition results in a decreased rate of immunogenicity loss during storage, the rate is not brought to zero. Simply put, storing a vaccine composition changes it. Thus, a trehalose-containing liquid vaccine composition according to the claimed invention that has been stored will necessarily be different from the same composition directly after it was prepared. Similarly, the vaccine composition of LaPosta that is lyophilized

[1] The rejection in paragraph 4 of the present Office Action sets forth the rejection as one under 35 U.S.C. § 103(a) and states that the rejection is the same as in paragraph 5 of the previous Office Action. But the rejection in the previous Office Action was under 35 U.S.C. § 102(e), and the discussion in the present Office Action relates to anticipation. Accordingly, the applicants presume the reference to 35 U.S.C. § 103(a) was in error and treat this as an anticipation rejection.

immediately after preparation will differ from one that is stored, as recited in the present claims. Hence, as the LaPosta composition is not stored and therefore necessarily different from the same composition that is stored according to the present claims, LaPosta cannot anticipate the present claims.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of claims 2-8, 11-15, and 17 under 35 U.S.C. § 103

Claims 2-8, 11-15, and 17 were newly rejected as obvious over Anderson *et al.*, in view of Samaritani, and further in view of Sola-Penna *et al.* In brief, the Office Action relies on Anderson *et al.* for its teaching of capsular polysaccharides conjugated to carrier proteins, Samaritani for its teaching that a non-reducing sugar for stabilization of pharmaceutical compositions to avoid lyophilization, and Sola-Penna *et al.* for its teaching of trehalose for the stabilization of macromolecules. For the following reasons, the applicants respectfully traverse.

The claims are not obvious over the cited art because the cited art fails both to provide the requisite particularized suggestion to make the presently claimed invention and to provide sufficient information from which the ordinary artisan could draw a reasonable expectation of success.

First, there is no suggestion or motivation in the cited art to make the presently claimed invention. Samaritani teaches the use of a non-reducing sugar generally and sucrose specifically to enhance the stability of liquid formulations comprising the protein hCG (human Chorionic Gonadotropin). Samaritani fails to provide any teachings or suggestions regarding the use of a non-reducing sugar for the stabilization of any other macromolecule, let alone an antigen comprising a polysaccharide conjugate to a carrier protein.

Sola-Penna *et al.* provides a study of trehalose as a stabilizer of "macromolecules," but the only macromolecules considered are enzymes and the stabilization studied was with respect to enzymatic activity. There is no teaching or suggestion in Sola-Penna *et al.* that trehalose would stabilize immunogenicity of an antigen.

Anderson *et al.* provides no teachings regarding stabilization of the disclosed polysaccharide-protein carrier conjugates.

The applicants respectfully submit that there is no suggestion or motivation in Anderson *et al.*, Samaritani, and/or Sola-Penna *et al.*, alone or together, to make the presently claimed composition. In support of the rejection, the Office Action makes the single, unsupported statement:

> It would be *prima facie* obvious at the time the invention was made to use trehalose to tabilize liquid composition comprising an antigen (polysaccharide bound to a carrier molecule) formulated in a liquid composition because Samaritani [teaches] that non-reducing sugars can be used to stabilize pharmaceutical compositions that are maintained in the liquid state and Sola-Penna *et al.* teach that trehalose is the best non-reducing sugar that can be used to stabilize macromolecules.

Office Action p. 6. But the present claims are not directed to pharmaceutical compositions generally comprising macromolecules. The present claims are directed to a pharmaceutical composition comprising a polysaccharide-protein conjugate, and none of Anderson *et al.*, Samaritani, and Sola-Penna *et al.* teach or suggest combining trehalose with such a conjugate to stabilize a vaccine composition. To render a claimed invention obvious, the prior art must provide a suggestion or motivation to make the particular invention being claimed, a general motivation is insufficient. *In re Deuel*, 34 U.S.P.Q.2d 1210, 1215 (Fed. Cir. 1995) (the prior art must suggest the particular form of the invention and how to make it; general guidance is insufficient); and *In re Obukowicz*, 27 U.S.P.Q.2d, 1063, 1065 (Bd. Pat. App. Int. 1992) (Prior art "that gives only general guidance and is not at all specific as to the particular form of the claimed invention and how to achieve it . . . does not make the invention obvious."). The cited art, each alone or all in combination fail to provide such a particularized suggestion.

Nor does the cited art provide sufficient teachings from which one of ordinary skill in the art could derive a reasonable expectation of success. Samaritani teaches only the combination of a non-reducing sugar generally and sucrose in particular for stabilizing the gonadotropin hCG to retain its activity, and Sola-Penna *et al.* teaches trehalose for stabilizing enzymes retain their enzymatic activity. None of Anderson *et al.*, Samaritani, and Sola-Penna *et al.*, alone or in combination, provide any teachings from which the ordinary artisan could derive an insight into the affects of trehalose on the immunogenicity of an antigen comprising a polysaccharide-protein conjugate. None of the art considers immunogenicity at all. Without such a teaching the present claims cannot be obvious.

Rejection of claims 9-10 and 16 under 35 U.S.C. § 103(a)

Claims 9-10 and 16 were rejected as obvious over Samaritani in view of Sola-Penna *et al.* and further in view of Anderson *et al.*, the same art as applied to claims 2-8, 11-15, and 17 in the previously discussed rejection. And for the same reasons presented above, the applicants respectfully traverse.

In brief, none of the cited art, alone or in combination teach or suggest the particular combination of trehalose with a polysaccharide-protein conjugate antigen. None recognize that trehalose can decrease the decay of immunogenicity of a polysaccharide-protein conjugate in a liquid vaccine composition. Samaritani teaches trehalose for stabilizing hCG and Sola-Penna *et al.* for stabilizing enzymatic activity. But a polysaccharide-protein conjugate has no such activities. So the benefits taught by Samaritani and Sola-Penna *et al.* relating to trehalose do not apply to a polysaccharide-protein conjugate and, therefore, cannot provide a suggestion or motivation to combine trehalose with a polysaccharide-protein conjugate.

Furthermore, without a recognition that trehalose can stabilize the immunogenicity of a polysaccharide-protein conjugate antigen, the ordinary artisan could not have had a reasonable expectation of success.

For these reasons at least, claims 9-10 and 16 cannot be obvious over the cited art. Accordingly, the applicants respectfully request reconsideration and withdrawal of this § 103 rejection.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of the pending § 102 and § 103 rejections. If there are any questions or comments regarding this response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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